

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended): Method for determining the presence of a genetic element such as a nucleotide repeat or a marker ~~genetic element(s), such as nucleotide repeat(s), or marker(s)~~ for microbial typing in a nucleic acid sample, which method comprises the steps of:
 - a) providing a the nucleic acid sample comprising a the genetic element(s);
 - b) providing an oligonucleotide(s) that is ~~are~~ completely or partially complementary to a the region(s) comprising the genetic element(s) of said nucleic acid sample;
 - c) annealing said oligonucleotide(s) to said nucleic acid sample;
 - d) ligating at least two of said oligonucleotides ~~said oligonucleotide(s)~~ annealed to said nucleic acid sample to each other using a ligase enzyme; and
 - e) detecting a ligation-by-product to determine whether a ligation reaction has occurred, as a measure of the presence of the genetic element(s),wherein steps a)-e) are performed simultaneously or subsequently or in any combination of subsequent steps.

2. (currently amended): Method for analysing the number of nucleotide repeats in a nucleic acid sample, which method comprises the steps of:
 - a) providing a nucleic acid sample potentially comprising a nucleotide repeat;
 - b) providing an oligonucleotide(s) complementary to said nucleotide repeat;
 - c) annealing said oligonucleotide(s) to said nucleic acid sample;
 - d) ligating at least two of said oligonucleotides ~~said oligonucleotide(s)~~ annealed to said nucleic acid sample to each other using a ligase enzyme; and
 - e) detecting a ligation by-product to determine whether a ligation reaction has occurred,wherein steps a)-e) are performed simultaneously or subsequently or in any combination of subsequent steps.

3. (currently amended): Method for analysing the number of nucleotide repeats in a nucleic acid sample, which method comprises the steps of:

- a) providing a nucleic acid sample potentially comprising a nucleotide repeat;
- b) providing an oligonucleotide(s) complementary to said nucleotide repeat;
- c) annealing said oligonucleotide(s) to said nucleic acid sample;
- d) ligating at least two of said oligonucleotides ~~said oligonucleotide(s)~~ annealed to said nucleic acid sample to each other using a ligase enzyme;
- e) converting a ligation by-product into ATP; and
- f) detecting said ATP to determine whether a ligation reaction has occurred, wherein steps a)-f) are performed simultaneously or subsequently or in any combination of subsequent steps.

4. (currently amended): Method for analysing the number of nucleotide repeats in a nucleic acid sample, which method comprises the steps of:

- a) providing a nucleic acid sample potentially comprising a nucleotide repeat;
- b) providing an oligonucleotide(s) complementary to said nucleotide repeat;
- c) annealing said oligonucleotide(s) to said nucleic acid sample;
- d) ligating at least two of said oligonucleotides ~~said oligonucleotide(s)~~ annealed to said nucleic acid sample to each other using a ligase enzyme;
- e) converting a ligation by-product into ATP; and
- f) detecting said ATP by a luciferase-based assay as a measure of whether a ligation reaction has occurred, wherein steps a)-f) are performed simultaneously or subsequently or in any combination of subsequent steps.

5. (currently amended): Method for microbial typing of a nucleic acid sample, which method comprises the steps of:

- a) providing a nucleic acid sample comprising at least one marker for microbial typing;
- b) providing an oligonucleotide that is ~~oligonucleotide(s) that are~~ completely or partially complementary to a ~~the~~ region(s) comprising a ~~a~~ marker(s) for microbial typing of said nucleic acid sample;
- c) annealing said oligonucleotide(s) to said nucleic acid sample;

d) ligating at least two of said oligonucleotides ~~said oligonucleotide(s)~~ annealed to said nucleic acid sample to each other using a ligase enzyme; and
e) detecting a ligation by-product to determine whether a ligation reaction has occurred; and
f) comparing the ligation pattern of the sample with a reference pattern in order to determine the microbial type,
wherein steps a)-e) are performed simultaneously or subsequently or in any combination of subsequent steps.

6. (currently amended): Method according to claim 1 ~~any one of claims 1-5~~ wherein an oligonucleotide ~~one of the oligonucleotides~~ in step b) is adapted to anneal immediately outside a ~~the~~ repeated sequence.

7. (currently amended): Method according to claim 1 ~~any one of claims 1-6~~ wherein the ligation by-product is AMP.

8. (currently amended): Method according to claim 1 ~~any one of claims 1-7~~ wherein step d) is performed employing a NAD⁺-dependent DNA-ligase.

9. (currently amended): Method according to claim 1 ~~any one of claims 1-8~~ wherein step e) is performed employing a pyruvate phosphate dikinase.

10. (currently amended): Method according to claim 1 ~~any one of claims 1-6~~, wherein step d) is performed employing an ATP-dependent ligase; and apyrase is added to the ligation mixture of step d) before, during or after ligation in order to reduce excess amounts of DNA ligase substrate.

11. (currently amended): Method according to claim 10, wherein the ATP dependent ligase is T4 DNA ligase.

12. (currently amended): Method according to claim 10 ~~or 11~~, wherein dATP is used as a substrate for the ATP dependent ligase in step d).

13. (currently amended): Method according to claim 1 ~~any one of claims 1-6 or 10-12~~, wherein the ligation by-product is pyrophosphate (PPi) ~~PPi~~.

14. (currently amended): Method according to claim 1 ~~any one of claims 1-6 or 10-13~~, wherein step e) is performed employing a ATP-sulfurylase.

15. (currently amended): Method according to claim 1 ~~any one of claims 1-14~~, wherein the oligonucleotide employed is a mono-, di- or multimer of the repeat ~~in itself~~.

16. (currently amended): Method according to claim 2 ~~any one of claims 1-14~~, wherein the oligonucleotide is ~~oligonucleotides are~~ complementary to, but that are out of phase with, said nucleotide repeat.

17. (currently amended): Method according to claim 16, further comprising a ~~step wherein unannealed oligonucleotides are removed after the detection by using an exonuclease~~
removing unannealed oligonucleotides with an exonuclease after the detection step.

18. (currently amended): Method according to claim 16, further comprising a ~~step wherein unannealed oligonucleotides are inactivated after the detection by using a phosphatase~~
inactivating unannealed oligonucleotide with a phosphatase after the detection step.

19. (currently amended): Method according to claim 1 ~~any one of claims 1-18~~, wherein the nucleic acid sample is immobilised on a support.

20. (currently amended): Method according to claim 19, further comprising a ~~step wherein unannealed oligonucleotides are removed after the detection by washing~~
removing unannealed oligonucleotides by washing after the detection step.

21. (currently amended): Method according to claim 1, ~~any one of claims 1-20~~, ~~preceded by a step wherein the nucleic acid sample is amplified~~

further comprising amplifying a nucleic acid sample prior to step a).

22. (currently amended): Method according to claim 4 ~~any one of claims 1-21~~, wherein the luciferase-based assay is a luminometric assay.

23. (currently amended): Method according to claim 4 ~~any one of claims 1-22~~, wherein ~~the~~ light that is produced in a ~~the~~ luciferase reaction is enzymatically turned off after an initial level of produced light has been reached.

24. (original): Method according to claim 23, wherein light production is turned off by the addition of apyrase.

25. (currently amended): Method according to claim 1, ~~wherein any one of claims 1-24~~ ~~where~~ oligonucleotides complementary to a region outside a region ~~that~~ to be analyzed are used to generate a signal by ligation or primer extension that can be used to normalize a ~~the~~ signal obtained from a ~~the~~ region to be analyzed.

26. (currently amended): Kit for performing the method according to claim 1 ~~any one of claims 1-25~~ comprising, in separate vials, a ligase enzyme and an enzyme for converting a ligation by-product into ATP.

27. (original): Kit according to claim 26 further comprising, in a separate vial, a luciferase enzyme.

28. (currently amended): Kit according to claim 26 ~~or 27~~, further comprising, in a separate vial, apyrase.

29. (currently amended): Kit according to claim 26 ~~any one of claims 26-28~~, further comprising oligonucleotides complementary to a nucleotide repeat, ~~optionally with an AdoPP5' modification~~, associated with a disease selected from the group consisting of following group of diseases: Dentatorubral pallidoluysian atrophy (DRPLA), Fragile X syndrome, Fragile site FRAXE, Huntington's disease, Kennedy's disease, Machado-Joseph disease, Myotonic dystrophy, Friedrich's

ataxia, Spinocerebellar ataxia type 1, Spinocerebellar ataxia type 2, Spinocerebellar ataxia type 3, Spinocerebellar ataxia type 6, Spinocerebellar ataxia type 8 and Spinocerebellar ataxia type 12.

30. (currently amended): Kit according to claim 26 ~~any one of claims 26-28~~, further comprising oligonucleotides complementary to a genetic region, ~~optionally with an AdoPP5' modification, that is~~ informative for identification of microbial species selected from the group consisting of: ~~from the following group:~~ the 16S rRNA gene, 23S rRNA gene, *groEL*, *gyrB*, *rpoB*, *rnpB*, and *groEL*, microsatellite sequences, and minisatellite sequences, VNTRs, the nuclear ribosomal DNA (rDNA) array – small-subunit (SSU) (18S-like), large-subunit (LSU)(23S, 26S, or 28S-like), 5.8S rRNA genes, and internal transcribed ribosomal DNA (rDNA) spacers (ITS1 and ITS2).

31. (currently amended): Composition comprising a ligase enzyme and an enzyme for converting a ligation by-product into ATP.

32. (currently amended): Composition according to claim 31 further comprising a luciferase enzyme.

33. (currently amended): Composition according to claim 31 ~~or 32~~ further comprising oligonucleotides complementary to a nucleotide repeat, ~~optionally with an AdoPP5' modification~~, associated with a disease selected from the group consisting of following group of diseases: Dentatorubral pallidoluysian atrophy (DRPLA), Fragile X syndrome, Fragile site FRAXE, Huntington's disease, Kennedy's disease, Machado-Joseph disease, Myotonic dystrophy, Friedrich's ataxia, Spinocerebellar ataxia type 1, Spinocerebellar ataxia type 2, Spinocerebellar ataxia type 3, Spinocerebellar ataxia type 6, Spinocerebellar ataxia type 8 and Spinocerebellar ataxia type 12.

34. (currently amended): Composition according to claim 31 ~~or 32~~ further comprising oligonucleotides complementary to a genetic region, ~~optionally with an AdoPP5' modification, that is~~ informative for identification of microbial species,

selected from the group consisting of ~~from the following group:~~ the 16S rRNA gene, 23S rRNA gene, *groEL*, *gyrB*, *rpoB*, *rnpB*, and *groEL*, microsatellite sequences, and minisatellite sequences, VNTRs, the nuclear ribosomal DNA (rDNA) array – small-subunit (SSU) (18S-like), large-subunit (LSU)(23S, 26S, or 28S-like), 5.8S rRNA genes, and internal transcribed ribosomal DNA (rDNA) spacers (ITS1 and ITS2).